

NON-TECHNICAL ABSTRACT

Fanconi's anemia is an inherited disorder that can produce bone marrow failure. In addition, some patients with Fanconi's anemia have physical defects, usually involving the skeleton or kidneys. The major problem for most patients is aplastic anemia. In aplastic anemia, the blood counts for red blood cells, white blood cells, and platelets are low because the bone marrow fails to produce these cells. Some patients with Fanconi's anemia also can develop leukemia or cancers in other organs. Many laboratory studies have suggested that Fanconi's anemia is due to an inherited defect in the ability of cells to repair DNA. Recently, the gene for one of the four types of Fanconi's anemia, type C, has been identified. It is known that this gene is defective in patients with Fanconi's anemia type C.

Studies in our laboratory have suggested that Fanconi's anemia type C may be a good candidate disease for gene therapy. We have placed the normal Fanconi's anemia type C gene into a retroviral vector and introduced the gene into cells, derived from Fanconi's anemia type C patients. In the laboratory, when we have compared cells lines and bone marrow cells from Fanconi's anemia patients before and after this procedure, we see a return towards normal of cell growth, resistance to the chemical agents that harm Fanconi's anemia cells, and a more normal appearance of the cells' chromosomes. Because the cells containing the normal Fanconi's anemia type C gene grow better, these cells should have a competitive advantage compared to unaltered Fanconi's anemia type C cells.

The purpose of this research protocol is to test whether we can safely introduce the normal Fanconi's anemia type C gene into stem cells of patients with this disease. Stem cells are the cells in the bone marrow and blood that give rise to the white cells, platelets, and red cells. We will treat blood cells from patients with Fanconi's anemia type C using the vector containing the Fanconi's anemia gene in a test tube and then return these cells to patients. If the cells are genetically altered, we expect to be able to detect the normal gene in blood and bone marrow cells afterwards. We hope that cells that contain the Fanconi's anemia gene will grow well in the bone marrow, and that we will be able to detect normal stem cells in special tissue culture studies. If we are successful, we should also be able to correct the chromosome abnormality. It may even be possible to increase blood counts in patients with Fanconi's anemia using this procedure. However, it should be clear that the major purpose of this protocol is to test the safety of this technique and to determine whether we can transfer the Fanconi's anemia gene successfully.

In order to obtain sufficient stem cells from patients with Fanconi's anemia, we will treat each patient with a hematopoietic growth factor called G-CSF or granulocyte-colony stimulating factor. G-CSF will be given for one week, at the end of which time blood cells will be removed by a process called apheresis for treatment with the Fanconi's anemia type C gene vector.